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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,084	06/08/2006	Claus Harder	117163.00137	8537

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EXAMINER	
FRAZIER, BARBARA S	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
02/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/535,084	HARDER ET AL.	
	Examiner	Art Unit	
	BARBARA FRAZIER	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4 and 7-18* is/are pending in the application.

4a) Of the above claim(s) *8,10,11 and 16-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,7,9 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/5/10 has been entered.

Status of Claims

1. Claims 4 and 7-18 are pending in this application.

2. Cancellation of claims 1-3 and 19-23 is acknowledged. Claims 5, 6, 24, and 25 already stand canceled.

3. Claims 4, 9-13, and 15-18 have been amended.

4. Claims 8, 10, 11, and 16-18 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/22/08.

5. Claims 4, 7, 9, and 12-15 are examined.

Claim Rejections - 35 USC § 112

6. The rejection of claims 4, 7, 9, 12, 13, and 15 under 35 U.S.C. 112, second paragraph is withdrawn in view of Applicant's amendments to claims 4, 9, 12, 13, and 15.

Claim Rejections - 35 USC § 103

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 4 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heublein et al (US 2002/0004060).

The claimed invention is drawn to an endoprosthesis comprising one or more of the elements from the group yttrium (Y), neodymium (Nd), or zirconium (Zr), wherein the endoprosthesis is adapted to be implanted in a vascular vessel and adapted to inhibit the proliferation of human smooth muscle cells of the vascular vessel wherein the formulation is adapted for intravascular liberation after implantation in a vascular vessel and the formulation includes an at least very substantially biodegradable carrier (see claim 4). Claim 7 is drawn to the a formulation as set forth in claim 4, wherein the carrier is an alloy, selected from the group consisting of magnesium, iron and tungsten alloys.

Heublein et al disclose a medical implant made of a metallic material (abstract), wherein the medical implant may be adapted for a vascular vessel, such as a stent (paragraphs 6 and 10). Vessel supports are able to overcome problems of a permanent

implant, including in-stent stenosis (paragraphs 31 and 7), and therefore are adapted to inhibit the proliferation of human smooth muscle cells of the vascular vessel. The implants are made of biodegradable material having at the same time advantageous mechanical properties (paragraph 11); said biodegradability reasonably reads on being adapted for "intravascular liberation" after implantation in a vascular vessel. Heublein et al further disclose that magnesium is preferred as the main constituent (paragraphs 13, 15, and 37), and advantageous decomposition times have furthermore been afforded by materials with magnesium as main constituent and rare earths as a secondary constituent; the rare earths may be present at 1-4%, in particular neodymium (paragraphs 15-21).

While Heublein et al do not specifically exemplify the combination of neodymium with a magnesium carrier, would have been obvious to a person having ordinary skill in the art at the time the invention was made to select neodymium with the magnesium carrier; thus arriving at the claimed invention (e.g., see paragraph 17). One skilled in the art would have been motivated to do so, with a reasonable expectation of success, because Heublein et al fairly teach and suggest advantageous decomposition times have been afforded by materials with magnesium as main constituent and 1-4% rare earths, in particular neodymium. Thus, it would be within the purview of the skilled artisan to select neodymium with the magnesium carrier, in order to optimize properties of the resultant formulation, such as decomposition times.

9. Claims 9 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heublein et al as applied to claims 4 and 7 above, and further in view of *The Columbia Electronic Encyclopedia*, 6th ed., 2007.

Claim 9 of the claimed invention is drawn to a formulation as set forth in claim 4, wherein the formulation contains Y in a quantitative proportion of between 3.7 and 5.5% by weight with respect to the total weight of the formulation (claim 9).

The invention of Heublein et al is delineated above (see paragraph 22). Heublein et al further teach that the formulation may contain 0- 5% rare earths (paragraphs 16-21).

Heublein et al do not teach that the rare earths may be yttrium.

However, one skilled in the art would reasonably envisage the use of yttrium from the disclosure of "rare earths" in Heublein et al. As evidence, *The Columbia Electronic Encyclopedia*, 6th ed., defines "rare earths" as a group of metals including yttrium (see citation at http://www.infoplease.com/ce6/sci/A0841162.html). Therefore, it would be within the purview of the skilled artisan to select yttrium as the rare earth in the formulation of Heublein et al by routine experimentation, in order to optimize the properties of the resultant formulation, including efficacy, stability, and rate of degradation. Regarding the amount of yttrium, the amount range of rare earth metal taught by Heublein et al overlaps that of the claimed invention; one skilled in the art would be motivated to manipulate the amount of yttrium from within said ranges by routine experimentation, in order to optimize the properties of the resultant formulation, including efficacy, stability, and rate of degradation.

Regarding claim 15, one skilled in the art would reasonably expect the formulation taught by Heublein et al to provide an yttrium concentration in the region of the human smooth muscle cells to be treated of between 200uM and 2 mM, as recited in the claimed invention, since the components and amounts taught in the formulation of Heublein et al are the same as those of the claimed invention.

10. Claims 9 and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heublein et al as applied to claims 4 and 7 above, and further in view of *The Columbia Electronic Encyclopedia* (6th ed., 2007), Tikhova et al (GB 1378281, cited by Applicants in IDS filed 7/16/09), Meyer-Lindenberg et al (US 2004/0241036, cited by Applicants in IDS filed 7/16/09), and ASM International Metals Handbook (Vol. 2, 1997, cited by Applicants in IDS filed 7/16/09, hereinafter "ASM Handbook").

The invention of claims 9 and 15 is delineated above (see paragraph 13). Claims 12-14 are further drawn to an endoprosthesis as set forth in claim 7, wherein the formulation is a magnesium alloy containing Y, rare earth without Y such as Nd, and remaining elements such as Zr, such as a WE43 alloy.

The invention of Heublein et al is delineated above (see paragraph 11). As noted above, "rare earths" includes yttrium (see paragraph 9, *supra*). Heublein et al further teach that one of the subsidiary constituents may be zirconium (paragraph 14). While Heublein et al generally teach the presence of rare earths in its magnesium-based alloy,

Heublein et al do not specifically teach the combination of yttrium, neodymium and zirconium.

Tikhova et al teach that magnesium-based alloys containing yttrium, neodymium and zirconium, in amounts comparable to that of the claimed invention, are known (col. 2, lines 43-48). Tikhova et al further teach that, due to the presence of yttrium and neodymium, the alloy exhibits favorable combination of high creep resistance and strength, leading to improved thermal stability (col. 2, lines 49-54), and zirconium is efficient for the formation of a fine-grained structure, which contributes not only to enhancement of mechanical properties in respect of short-term stress but to substantial improvement in technological casting properties of the alloy (col. 2, lines 55-60).

Meyer-Lindenberg et al teach a medical implant for the body consisting at least partially of a magnesium alloy (abstract). The implant can be degraded by the body with no or only minor side effects (paragraph 6). Meyer-Lindenberg et al teach that the addition of rare earth metals to magnesium-based alloys improves their mechanical material properties, including increased ductility and increased strength accompanied by good corrosion resistance (paragraph 8). Meyer-Lindenberg et al specifically teach that a Mg-Y-Nd-Zr alloy has the same corrosion rate as the reference alloy AZ91, but has a reduced pitting depth, and Y and Nd are recommended as corrosion-protection in the alloy (paragraph 29).

ASM Handbook teaches that the alloy WE43 is a known Mg-Y-Nd-Zr alloy (disclosure).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to use a Mg-Y-Nd-Zr alloy such as WE43 in the implant of Heublein et al; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because the use of said magnesium-based alloy provides the advantageous properties of high creep resistance and strength, improved thermal stability, enhancement of mechanical properties in respect of short-term stress and improved technological casting properties of the alloy, as taught by Tikhova et al. Additionally, the use of a Mg-Y-Nd-Zr alloy provides the benefits of corrosion resistance and reduced pitting depth, as well as good strength and biodegradability, as taught by Meyer-Lindenberg et al. One would reasonably expect success from the use of a Mg-Y-Nd-Zr alloy such as a WE43 alloy in the implant of Heublein et al because Heublein et al fairly teach and suggest that its magnesium-based alloys may contain rare earths, as well as zirconium and neodymium.

Regarding claim 15, one skilled in the art would reasonably expect the formulation taught by the combined references to provide an yttrium concentration in the region of the human smooth muscle cells to be treated of between 200uM and 2 mM, as recited in the claimed invention, since the components and amounts taught in the formulation of the combined references are the same as those of the claimed invention.

Response to Arguments

11. Applicant's arguments filed 1/5/10 have been fully considered but they are not persuasive.

In response to Applicant's arguments that Heublein provides no actual guidance as to advantages or disadvantages of components in the alloy, it is noted that Heublein specifically teach magnesium with one of only six preferred embodiments, three of which contain rare earths, particularly neodymium as a choice of four rare earths (paragraphs 16-21). Therefore, one skilled in the art has reasonable guidance to select neodymium with magnesium in the medical implant of Heublein et al.

In response to Applicant's arguments regarding a) the presence or absence of lithium in the alloy, and b) other metals or rare earths in the alloy, it is noted that a) Applicant's use of the open-ended term "comprising" allows for the presence of other metals, including lithium, in the alloy, and b) Heublein et al specifically teach that one of the preferred embodiments comprises 1-4% rare earths, with neodymium as one of only four preferred choices (paragraph 17), and therefore one skilled in the art would be reasonably guided to select neodymium in the alloy.

In response to Applicant's arguments regarding the presence of zirconium in the alloy, it is noted that zirconium is one of about 20 choices for the subsidiary constituent with magnesium or iron (paragraphs 13 and 14), and thus it would be within the purview of the skilled artisan to select zirconium with magnesium or iron by routine experimentation. Even so, it is noted that claims 4 and 7 only require the presence of a single metal with the magnesium alloy, and therefore the presence of zirconium with neodymium or yttrium is not required in the rejection over Heublein alone. In the claims where zirconium is required with yttrium and neodymium (claims 12-14), the

combination of references meets the limitations of the claims, for reasons stated above (see paragraph 10, *supra*).

In response to Applicant's arguments regarding the rejection of claims 9 and 15, it is noted that Heublein specifically teach magnesium with one of only six preferred embodiments, three of which contain rare earths, and *The Columbia Electronic Encyclopedia*, 6th ed., defines "rare earths" as a group of metals including yttrium:

> "**rare-earth metals**, in chemistry, group of metals including those of the lanthanide series and actinide series, usually yttrium"

Therefore, one skilled in the art would be reasonably guided to select yttrium as the rare earth metal. Additionally, regarding claim 15, one skilled in the art would reasonably expect the formulation taught by Heublein et al to provide an yttrium concentration in the region of the human smooth muscle cells to be treated of between 200uM and 2 mM, as recited in the claimed invention, since the components and amounts taught in the formulation of Heublein et al are the same as those of the claimed invention.

In response to Applicant's arguments that the alloys of Tikhova and ASM have different applications than the medical field, and do not teach that the alloys are biocompatible, it is noted that Tikhova and ASM are relied upon to show the positive properties of the alloy, which would be considered capable of use as an endoprosthesis based on the teachings of Heublein. Additionally, Meyer-Lindenberg et al specifically teach that Mg-Y-Nd-Zr alloys are useful as medical implants and are biodegradable, and therefore one skilled in the art would find such alloys capable of use as an endoprosthesis based on the teachings of the combined references.

In response to Applicant's arguments that the ASM reference does not teach WE43, it is not clear why Applicants take this position, as the reference was supplied by Applicants and clearly teaches the WE43 alloy (see NPL reference #10 from Applicant's IDS filed 7/16/09).

Therefore, it is the Examiner's position that the claims are rendered obvious.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

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